This Week's Citation Classic ®

Robertus J D, Ladner J E, Finch J T, Rhodes D, Brown R S, Clark B F C & Klug A. Structure of yeast phenylalanine tRNA at 3Å resolution. *Nature* 250:546-51, 1974.
[MRC Laboratory of Molecular Biology, Cambridge, England]

The three-dimensional structure of $tRNA^{Phe}$ was determined by X-ray diffraction. The double helices predicted from the cloverleaf model are seen, together with single strand stacking and novel base interactions. [The *SCI*® indicates that this paper has been cited in more than 430 publications.]

The Tertiary Structure of tRNA

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I was originally drawn to Aaron Klug's laboratory at the MRC in Cambridge because of his brilliant work on three-dimensional reconstruction from electron micrographs. (It was for this work that he won the 1982 Nobel Prize in chemistry.) When I arrived in July 1972 from San Diego, I got two surprises. The first was the temperature; *The London Times* carried a headline decrying a local heat wave, "72 Again Tomorrow, No Relief in Sight." Clearly there would be no surfing here. The second surprise was that Klug's group had just obtained crystals of yeast $tRNA^{Phe}$, and my project was to solve the structure. At the time, tRNA was probably the hottest topic in structural biochemistry, since no single crystal structure for nucleic acids existed. Needless to say, the competition to be first was ferocious.

Alex Rich and his group at the Massachusetts Institute of Technology (MIT), Cambridge, had obtained another crystal form of the same molecule and even had a low resolution image of it, so we were clearly behind. Nevertheless, Klug's group was a good one, including Jane E. Ladner, Daniella Rhodes, Ray S. Brown, and his longtime associate John T. Finch.

The importance of the structure and the excitement of competition drove our crew along. We enjoyed the work and developed a strong group loyalty; I remember those days as among the most enjoyable of my life. In 18 months, we produced a 3Å electron density map. The interpretation was difficult, and I spent uncounted hours in front of the six-foot, half-silvered mirror we used to construct the model. By March of 1974, we had finished the model and its description was published at the same time as a revised MIT structure.[1] Initially, there were some minor disagreements about details of the models,[2] but both groups are credited today with the "first" tRNA structure.

In addition to defining the basic fold for the entire class of molecules, we were able to define a number of novel base interactions that secured the joints between double helices.[3] Presumably, interactions of this type are used to build structures like rRNA.

Since our original work, several other tRNA structures have been solved, confirming that all fit the basic pattern. Furthermore, a number of amino acyl tRNA synthetase structures have been solved, including that for glutamine, which had its cognate tRNA bound.[4] Structures like this are helping to lay down rules for the way proteins and nucleic acids interact at the atomic level and will increase our understanding of the control of living chemistry.

1. **Kim S H, Suddath F L, Quigley G J, McPherson A, Sussman J L, Wang A H J, Seeman N C & Rich A.** Three-dimensional tertiary structure of yeast phenylalanine transfer RNA. *Science* 185:435-40, 1974. (Cited 395 times.)
2. **Klug A, Robertus J D, Ladner J E, Brown R S & Finch J T.** Conservation of the molecular structure of yeast phenylalanine transfer RNA in two crystal forms. *Proc. Nat. Acad. Sci. USA* 71:3711-5, 1974.
3. **Klug A, Ladner J & Robertus J D.** The structural geometry of coordinated base changes in transfer RNA. *J. Mol. Biol.* 89:511-6, 1974. (Cited 60 times.)
4. **Rould M A, Perona J J, Soll D & Steitz T A.** Structure of *E. coli* glutaminyl-tRNA synthetase complexed with $tRNA^{Gln}$ and ATP at 2.8Å resolution. *Science* 246:1135-42, 1990.

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